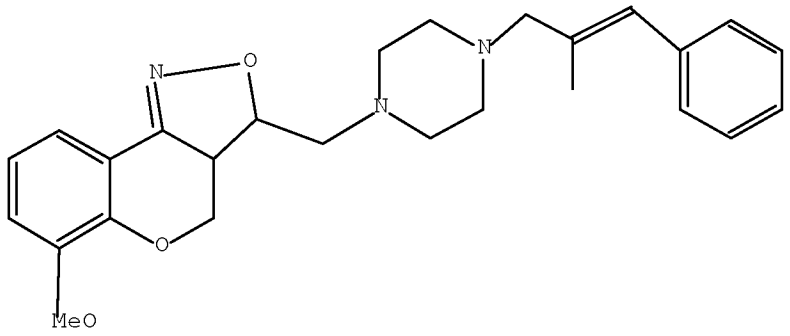
***** QUERY RESULTS *****

=> d his l26

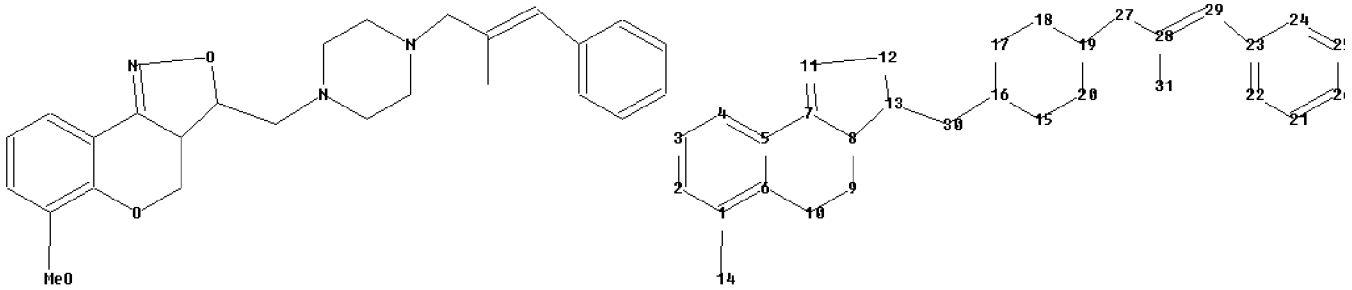
(FILE 'HCAPLUS' ENTERED AT 14:49:39 ON 21 FEB 2008)
L26 3 S L25

=> d que l26
L4 STR



Structure attributes must be viewed using STN Express query preparation:

Uploading L2.str

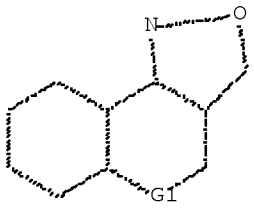


chain nodes :
14 27 28 29 30 31
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 15 16 17 18 19 20 21 22 23 24
25 26
chain bonds :
1-14 13-30 16-30 19-27 23-29 27-28 28-29 28-31
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 7-11 8-9 8-13 9-10 11-12 12-13
15-16 15-20 16-17 17-18 18-19 19-20 21-22 21-26 22-23 23-24 24-25 25-26
exact/norm bonds :
5-7 6-10 7-8 7-11 8-9 8-13 9-10 11-12 12-13 15-16 15-20 16-17 16-30
17-18 18-19 19-20 19-27
exact bonds :
1-14 13-30 23-29 27-28 28-29 28-31
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 21-22 21-26 22-23 23-24 24-25 25-26

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:CLASS 15:Atom 16:Atom 17:CLASS 18:Atom 19:Atom
20:Atom 21:Atom
22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:CLASS 28:CLASS 29:CLASS 30:CLASS
31:CLASS

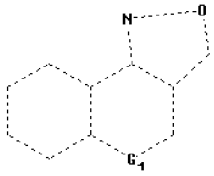
L12 STR

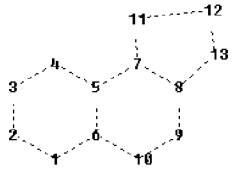


G1 O,S,N,CH2

Structure attributes must be viewed using STN Express query preparation:

Uploading L4.str





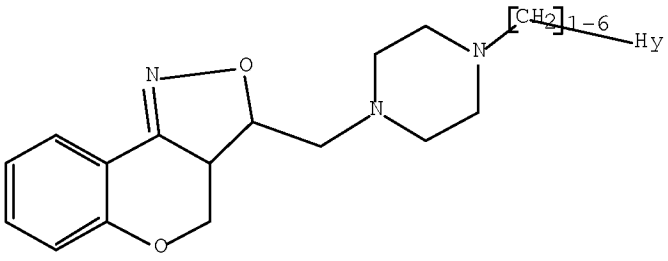
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 7-11 8-9 8-13 9-10 11-12 12-13

exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 7-11 8-9 8-13 9-10 11-12 12-13

G1:O,S,N,CH2

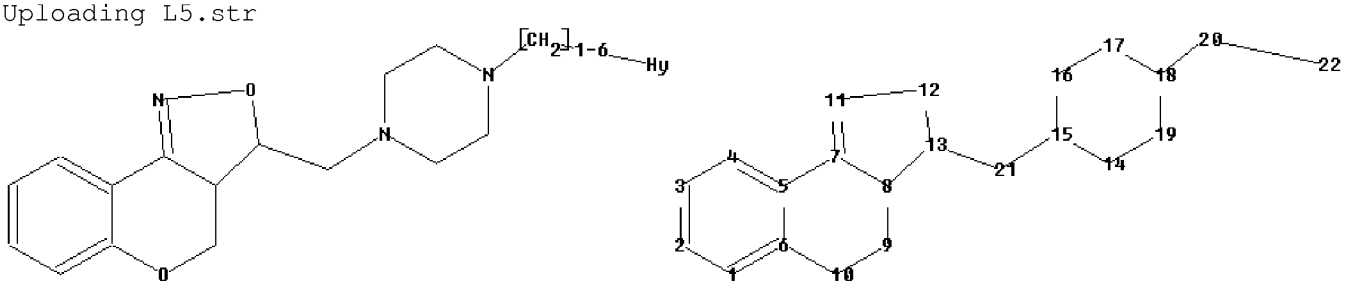
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom

L15 2772 SEA FILE=REGISTRY SSS FUL L12
L23 STR



Structure attributes must be viewed using STN Express query preparation:

Uploading L5.str



chain nodes :
20 21 22
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
chain bonds :
13-21 15-21 18-20 20-22
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 7-11 8-9 8-13 9-10 11-12 12-13
14-15 14-19 15-16 16-17 17-18 18-19
exact/norm bonds :
5-7 6-10 7-8 7-11 8-9 8-13 9-10 11-12 12-13 14-15 14-19 15-16 15-21
16-17 17-18 18-19 20-22
exact bonds :
13-21 18-20
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:Atom 18:Atom 19:Atom
20:CLASS 21:CLASS
22:Atom

L25 37 SEA FILE=REGISTRY SUB=L15 SSS FUL (L4 OR L23)

L26 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L25

=> d l26 ibib ed abs hitstr hitind 1-3

L26 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:182889 HCAPLUS Full-text
DOCUMENT NUMBER: 140:235700
TITLE: Preparation of chromenoisoxazole derivatives and their use as anti-depressants
INVENTOR(S): Andres-Gil, Jose Ignacio; Alcazar-Vaca, Manuel Jesus; Matesanz-Ballesteros, Maria Encarnacion; Bakker, Margaretha Henrica Maria; Megens, Antonius Adrianus Hendrikus Petrus
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018482	A2	20040304	WO 2003-EP9532	20030819
WO 2004018482	A3	20040401		
WO 2004018482	A8	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2495058	A1	20040304	CA 2003-2495058	20030819
AU 2003271567	A1	20040311	AU 2003-271567	20030819
EP 1532155	A2	20050525	EP 2003-753363	20030819
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1675223	A	20050928	CN 2003-819862	20030819
JP 2005538143	T	20051215	JP 2004-530256	20030819
US 2006122167	A1	20060608	US 2005-524989	20050218

PRIORITY APPLN. INFO.: EP 2002-78844 A 20020821
WO 2003-EP9532 W 20030819
OTHER SOURCE(S): MARPAT 140:235700
ED Entered STN: 05 Mar 2004
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X = CH2, NR7, S or O; R7 = H, alkyl, (un)substituted- aryl, -arylalkyl; R1, R2, R14, R15 = independently H, halo, OH, alkyloxy, CN, etc.; m = 1-4; R3 = (un)substituted aromatic homocyclic or heterocyclic ring; R8 = independently OH, amino, nitro, CN, halo, or alkyl; n = 0-5; R9 = H, alkyl, or

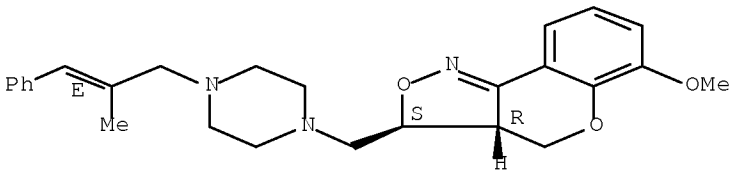
formyl], a process for their preparation, pharmaceutical compns. comprising them and their use as a medicine, in particular for the treatment of depression, anxiety, movement disorders, psychosis, Parkinson's disease and body weight disorders is disclosed. Thus, e.g., II, was prepared by substitution of 6-bromo-7,8-dimethoxy-3-[4-(2-methyl-3- phenylallyl)piperazin-1-ylmethyl]-3a,4-dihydro-3H-chromeno[4,3-c]isoxazole (preparation given) with N-methylpiperazine. The compds. according to the invention have surprisingly been shown to have a serotonin (5-HT) reuptake inhibitor activity in combination with addnl. α2-adrenoceptor antagonist activity and show a strong anti-depressant activity without being sedative. I produced an inhibition at least at the hα2A site (but often at the hα2B and hα2C sites) and simultaneously at the 5-HT transporter site of more than 50 % (pIC50) at a test concentration ranging between 10-6 M and 10-9 M in a concentration-dependent manner. The invention also relates to novel combination of isoxazoline derivs. according to the invention with one or more other compds. selected from the group of antidepressants, anxiolytics, anti-psychotics and anti-Parkinson's disease drugs to improve efficacy and/or onset of action.

IT 667454-39-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of chromenoisoxazole derivs. as antidepressants)

RN 667454-39-9 HCAPLUS

CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-6-methoxy-3-[[4-[(2E)-2-methyl-3-phenyl-2-propenyl]-1-piperazinyl]methyl]-, (3R,3aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



IC ICM C07D498-04
ICS A61K031-424; A61P025-00

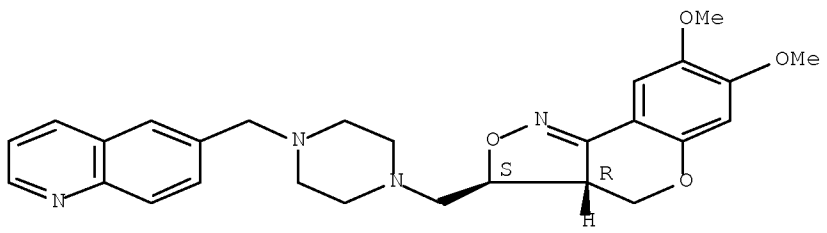
CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT 667454-35-5P 667454-39-9P 667454-52-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of chromenoisoxazole derivs. as antidepressants)

L26 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:535065 HCAPLUS Full-text
DOCUMENT NUMBER: 139:292184
TITLE: Synthesis of 3a,4-dihydro-3H-[1]benzopyrano[4,3-c]isoxazoles, displaying combined 5-HT uptake inhibiting and α2-adrenoceptor antagonistic activities: a novel series of potential

antidepressants
AUTHOR(S): Andres, J. Ignacio; Alcazar, Jesus; Alonso, Jose M.; Alvarez, Rosa M.; Cid, Jose M.; De Lucas, Ana I.; Fernandez, Javier; Martinez, Sonia; Nieto, Carmen; Pastor, Joaquin; Bakker, Margot H.; Biesmans, Ilse; Heylen, Lieve I.; Megens, Anton A.
CORPORATE SOURCE: Division of Janssen-Cilag, Medicinal Chemistry Department, Jarama s/n, Johnson & Johnson Pharmaceutical Research & Development, Toledo, 45007, Spain
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(16), 2719-2725
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:292184
ED Entered STN: 14 Jul 2003
AB The synthesis of a series of novel 3-piperazinylmethyl-3a,4-dihydro-3H-[1]benzopyrano[4,3-c]isoxazoles as novel dual 5-HT re-uptake inhibitors and α2-adrenoceptor antagonists is described. Their affinity at the three different human α2-adrenoceptor subtypes and the 5-HT transporter site is reported. The in vivo activity of the compds. was measured in two different assays: (1) inhibition of pCA-induced excitation, which evaluates the ability to block the central 5-HT transporter, and (2) inhibition of xylazine-induced loss of righting, which evaluates the ability to block central α2-adrenoceptors. Compds. thus prepared included (3R,3aS)-rel-3a,4-dihydro-3-[[4-[(2E)-3- phenyl-2-propenyl]-1-piperazinyl]methyl]-3H-[1]benzopyrano[4,3-c]isoxazole, (3R,3aS)-rel-(-)-3a,4-dihydro-8-methoxy-3-[[4-[(2E)-3-phenyl- 2-propenyl]-1-piperazinyl]methyl]-3H-[1]benzopyrano[4,3-c]isoxazole, (3R,3aS)-rel-(+)-3a,4-dihydro-8-methoxy-3-[[4-[(2E)-3-phenyl-2-propenyl]-1-piperazinyl]methyl]-3H-[1]benzopyrano[4,3-c]isoxazole and derivs. thereof.
IT 452313-43-8P 452316-09-5P 452316-15-3P 608146-10-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of dihydro[1]benzopyrano[4,3-c]isoxazoles and their activity as
5-HT uptake inhibitors and α2-adrenoceptor antagonists (potential antidepressants))
RN 452313-43-8 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-7,8-dimethoxy-3-[[4-(6-quinolinylmethyl)-1-piperazinyl]methyl]-, (3R,3aS)-rel- (CA INDEX NAME)

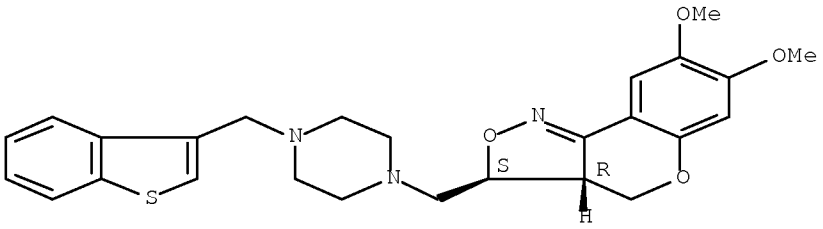
Relative stereochemistry.



RN 452316-09-5 HCAPLUS

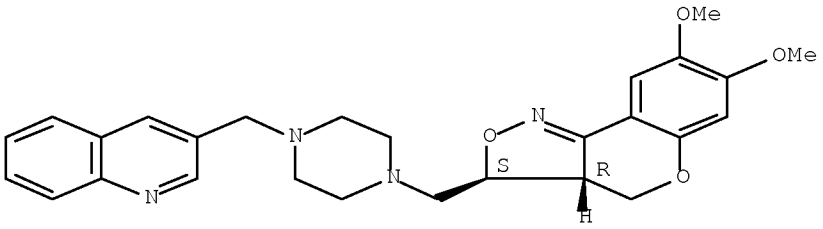
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-(benzo[b]thien-3-ylmethyl)-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



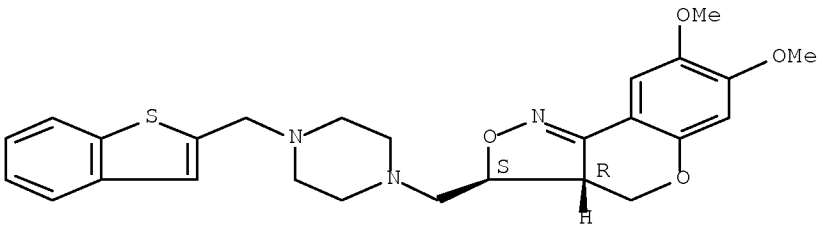
RN 452316-15-3 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-7,8-dimethoxy-3-[[4-(3-quinolinylmethyl)-1-piperazinyl]methyl]-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



RN 608146-10-7 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-(benzo[b]thien-2-ylmethyl)-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT 452313-36-9P 452313-43-8P 452313-54-1P 452313-56-3P

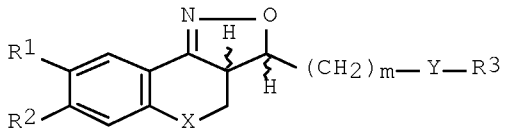
452313-77-8P 452314-18-0P 452316-09-5P 452316-15-3P
452316-21-1P 452316-33-5P 452316-36-8P 452316-66-4P 452316-84-6P
452318-20-6P 452318-24-0P 452318-26-2P 452318-93-3P 452318-95-5P
452318-97-7P 452319-25-4P 452319-35-6P 452320-01-3P
608146-10-7P 608146-11-8P 608146-12-9P 608146-13-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of dihydro[1]benzopyrano[4,3-c]isoxazoles and their activity as
5-HT uptake inhibitors and α2-adrenoceptor antagonists (potential antidepressants))
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:658130 HCAPLUS Full-text
DOCUMENT NUMBER: 137:201298
TITLE: Preparation of substituted isoxazolines as anti-depressants
INVENTOR(S): Andres-Gil, Jose Ignacio; Fernandez-Gadea, Francisco Javier; Alcazar-Vaca, Manuel Jesus; Cid-Nunez, Jose Maria; Pastor-Fernandez, Joaquin; Megens, Antonius Adrianus Hendrikus Petrus; Heylen, Godelieve Irma Christine Maria; Langlois, Xavier Jean Michel; Bakker, Margaretha Henrica Maria; Steckler, Thomas Horst Wolfgang
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

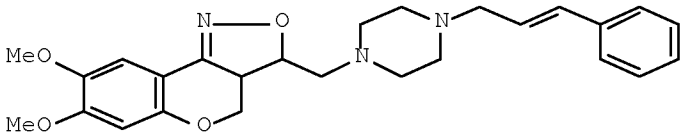
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066484	A1	20020829	WO 2002-EP1567	20020213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2437505	A1	20020829	CA 2002-2437505	20020213
AU 2002244717	A1	20020904	AU 2002-244717	20020213
AU 2002244717	B2	20070719		
EP 1368358	A1	20031210	EP 2002-712909	20020213
EP 1368358	B1	20060823		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200300398	A	20031215	EE 2003-398	20020213
HU 2003003270	A2	20040128	HU 2003-3270	20020213
HU 2003003270	A3	20070328		
CN 1492871	A	20040428	CN 2002-805243	20020213
NZ 526741	A	20040430	NZ 2002-526741	20020213
BR 2002007433	A	20040601	BR 2002-7433	20020213
JP 2004518748	T	20040624	JP 2002-565998	20020213

JP 3953424	B2	20070808			
AT 337322	T	20060915	AT 2002-712909		20020213
ES 2271230	T3	20070416	ES 2002-712909		20020213
TW 257392	B	20060701	TW 2002-91102853		20020220
IN 2003DN00968	A	20070525	IN 2003-DN968		20030624
BG 107984	A	20040930	BG 2003-107984		20030708
MX 2003PA07432	A	20031118	MX 2003-PA7432		20030819
NO 2003003700	A	20031021	NO 2003-3700		20030820
ZA 2003006487	A	20041122	ZA 2003-6487		20030820
US 2004122037	A1	20040624	US 2003-468555		20030821
US 7169786	B2	20070130			
PRIORITY APPLN. INFO.:			EP 2001-200611	A	20010221
			EP 2001-201264	A	20010405
			WO 2002-EP1567	W	20020213

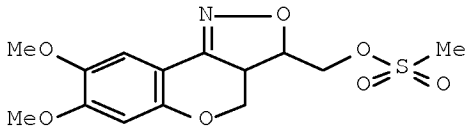
OTHER SOURCE(S): MARPAT 137:201298
ED Entered STN: 30 Aug 2002
GI



I



II



III

AB Title compds. I [wherein X = CH2, NR7, S or O; R7 = H, (un)substituted alkyl, Ph, Ph alkyl, etc.; R1 and R2 independently = H, OH, CN, halo, OSO2H, (un)substituted Ph, phenylalkyl, alkoxy, etc.; or R1 and R2 may be taken together to form a bivalent radical selected from -CH2CH2O-, -OCH2CH2-, -OCH2O-, -CH2OCH2- and -OCH2CH2O-; m = 1-4; Y = (un)substituted piperidyl or piperazyl radical and R3 represents an (un)substituted aromatic homocyclic or heterocyclic ring system including a partially or completely hydrogenated hydrocarbon chain of maximum 6 atoms long with which the ring system is attached to the Y radical and which may contain one or more heteroatoms selected from the group of O, N and S], a process for their preparation, pharmaceutical compns. comprising them and their use as a medicine for treating anxiety disorders and disorders of body weight are disclosed. Thus, II was prepared in 60% yield by reaction of III with N-(3-phenyl-2-propenyl)-piperazine. III was prepared by substitution of Me 4-bromo-2-butenoate with 2-hydroxy-4,5-dimethoxybenzaldehyde with subsequent condensation with hydroxylamine, cyclization, reduction and sulfonation with methanesulfonyl

chloride. The compds. according to the invention have surprisingly been shown to have a serotonin (5-HT) reuptake inhibitor activity in combination with addnl. α2-adrenoceptor antagonist activity and show a strong anti-depressant activity without being sedative. I produced an inhibition at the hα2A site (but often also at the hα2B and hα2C sites) and simultaneously at the 5-HT transporter site of more than 50% (pIC50) at a test concentration ranging between 10-6 M and 10-9 M in a concentration dependent manner. The invention also relates to novel combination of substituted isoxazolines derivs. having anti-depressant activity and/or anxiolytic activity and/or body weight control activity with antidepressants, anxiolytics and/or antipsychotics to improve efficacy and/or onset of action.

IT 452313-43-8P 452314-95-3P 452314-98-6P
452315-01-4P 452315-04-7P 452315-07-0P
452315-10-5P 452315-13-8P 452315-16-1P
452315-19-4P 452315-22-9P 452315-24-1P
452315-27-4P 452315-30-9P 452315-33-2P
452315-94-5P 452315-97-8P 452316-00-6P
452316-03-9P 452316-06-2P 452316-09-5P
452316-12-0P 452316-15-3P 452316-18-6P
452316-24-4P 452316-39-1P 452316-58-4P
452316-64-2P 452318-91-1P 452319-17-4P
452934-93-9P 452934-94-0P

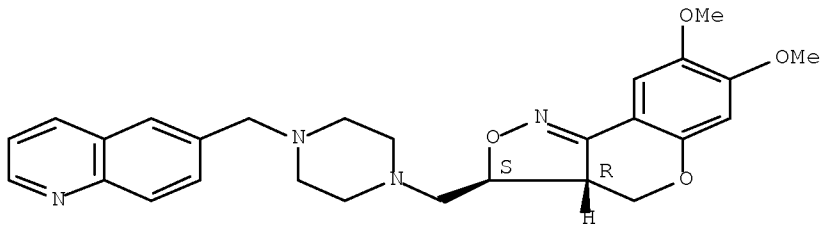
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compound; preparation and pharmaceutical activity of substituted isoxazolines as anti-depressants)

RN 452313-43-8 HCAPLUS

CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-7,8-dimethoxy-3-[[4-(6-quinolinylmethyl)-1-piperazinyl]methyl]-, (3R,3aS)-rel- (CA INDEX NAME)

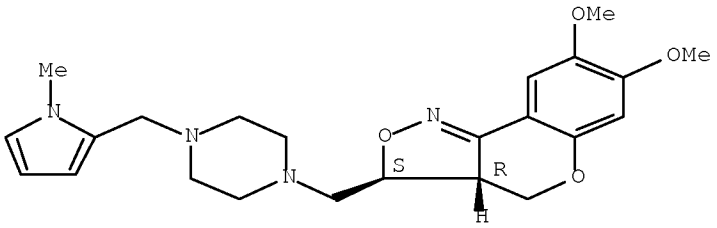
Relative stereochemistry.



RN 452314-95-3 HCAPLUS

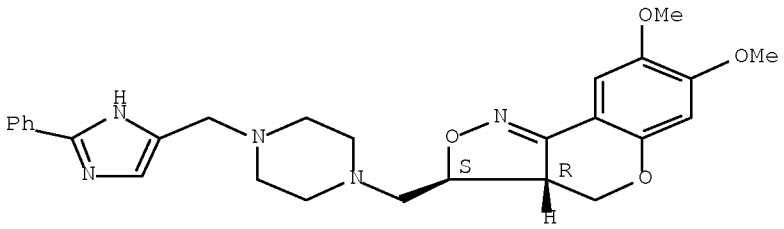
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-7,8-dimethoxy-3-[[4-[(1-methyl-1H-pyrrol-2-yl)methyl]-1-piperazinyl]methyl]-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



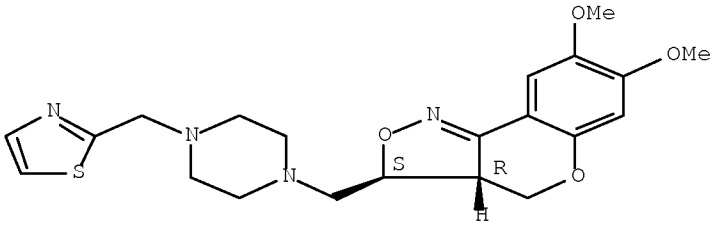
RN 452314-98-6 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-7,8-dimethoxy-3-[[4-[(2-phenyl-1H-imidazol-4-yl)methyl]-1-piperazinyl]methyl]-, (3R,3aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



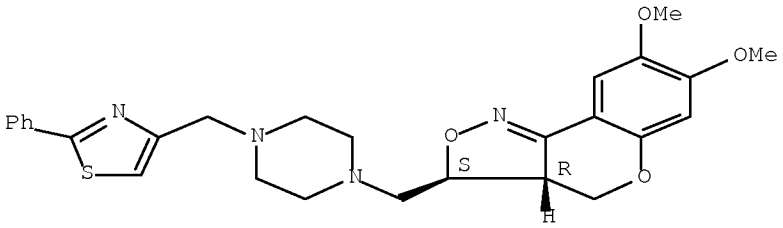
RN 452315-01-4 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-7,8-dimethoxy-3-[[4-(2-thiazolylmethyl)-1-piperazinyl]methyl]-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



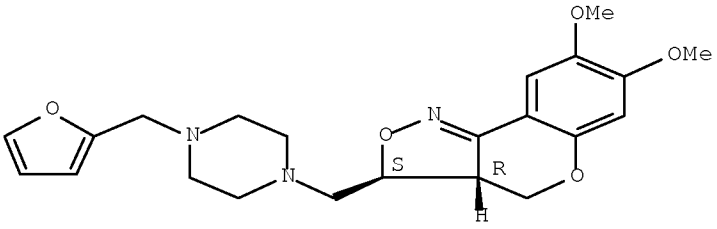
RN 452315-04-7 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-7,8-dimethoxy-3-[[4-[(2-phenyl-4-thiazolyl)methyl]-1-piperazinyl]methyl]-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



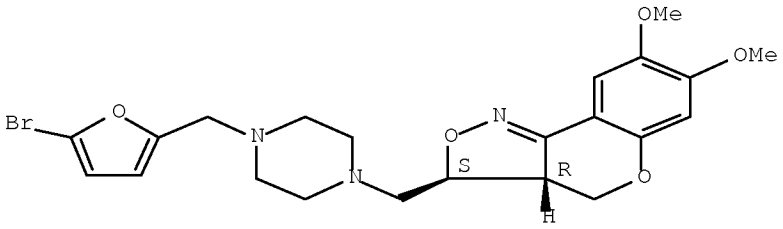
RN 452315-07-0 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-(2-furanylmethyl)-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



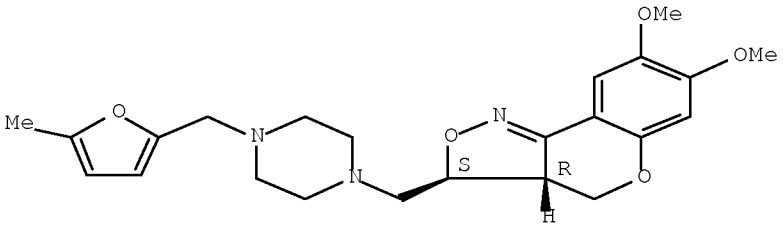
RN 452315-10-5 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-[(5-bromo-2-furanyl)methyl]-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



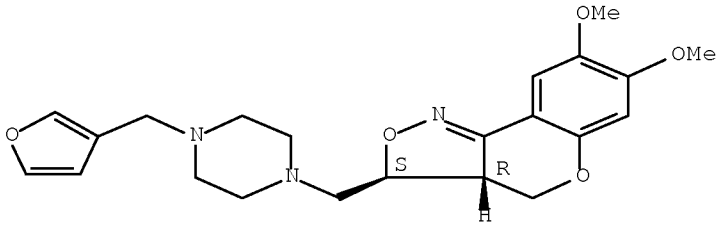
RN 452315-13-8 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-7,8-dimethoxy-3-[[4-[(5-methyl-2-furanyl)methyl]-1-piperazinyl]methyl]-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



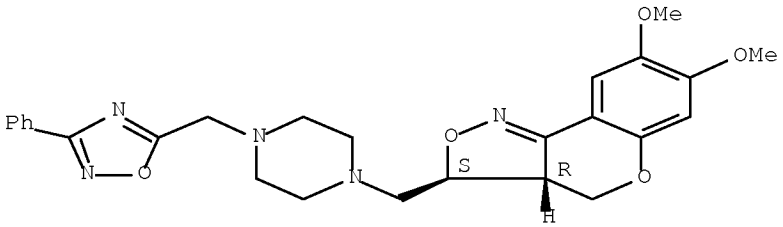
RN 452315-16-1 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-(3-furanylmethyl)-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



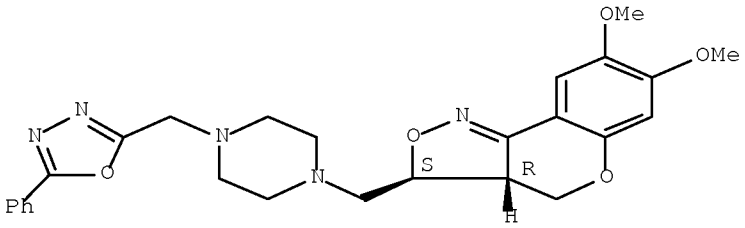
RN 452315-19-4 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-7,8-dimethoxy-3-[[4-[(3-phenyl-1,2,4-oxadiazol-5-yl)methyl]-1-piperazinyl]methyl]-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



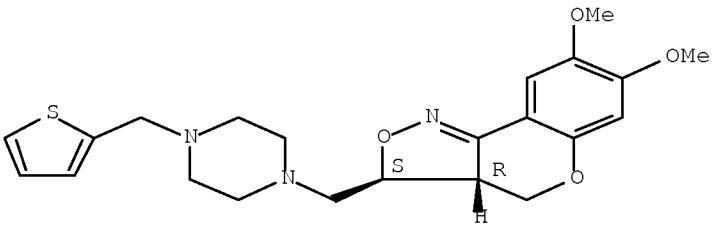
RN 452315-22-9 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-7,8-dimethoxy-3-[[4-[(5-phenyl-1,3,4-oxadiazol-2-yl)methyl]-1-piperazinyl]methyl]-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



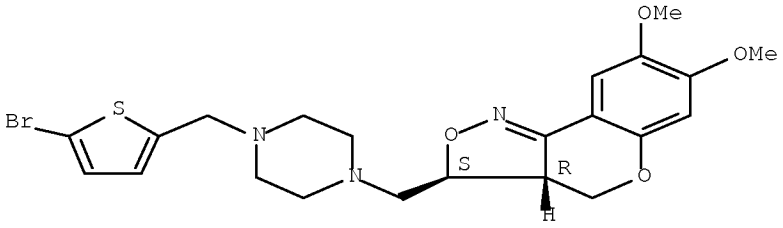
RN 452315-24-1 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-7,8-dimethoxy-3-[[4-(2-thienylmethyl)-1-piperazinyl]methyl]-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



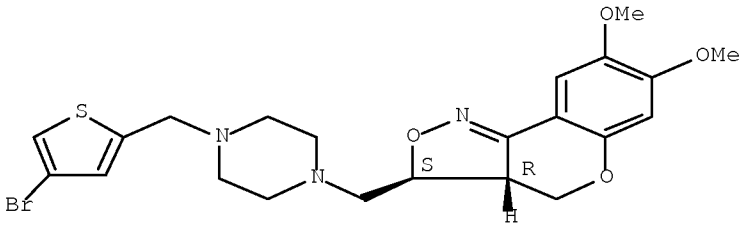
RN 452315-27-4 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-[(5-bromo-2-thienyl)methyl]-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



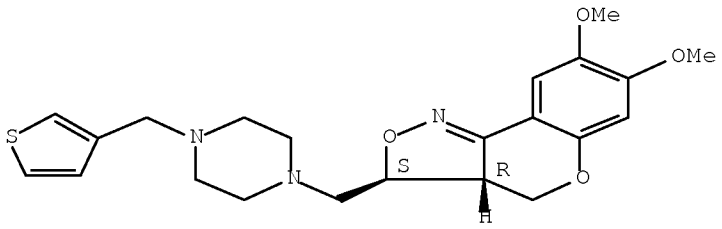
RN 452315-30-9 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-[(4-bromo-2-thienyl)methyl]-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



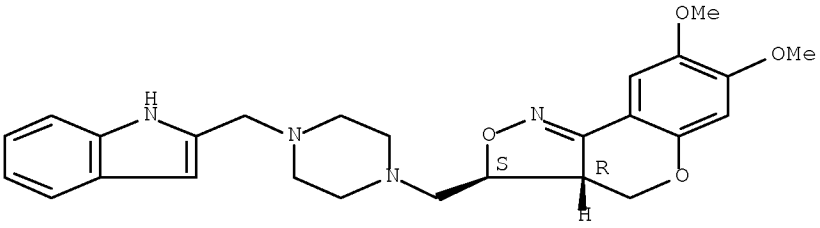
RN 452315-33-2 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-7,8-dimethoxy-3-[[4-(3-thienylmethyl)-1-piperazinyl]methyl]-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



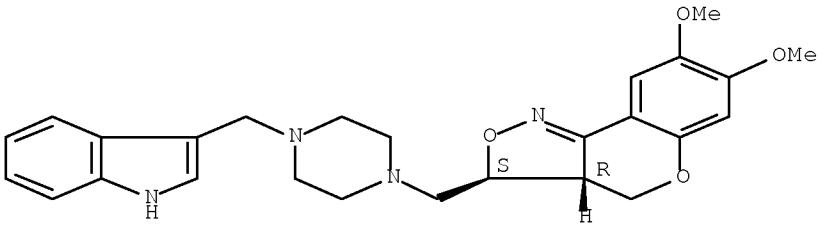
RN 452315-94-5 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-3-[[4-(1H-indol-2-ylmethyl)-1-piperazinyl]methyl]-7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



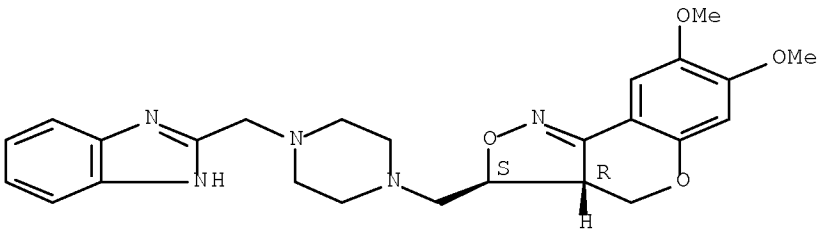
RN 452315-97-8 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-3-[[4-(1H-indol-3-ylmethyl)-1-piperazinyl]methyl]-7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



RN 452316-00-6 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-(1H-benzimidazol-2-ylmethyl)-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, dihydrochloride, (3R,3aS)-rel- (9CI) (CA INDEX NAME)

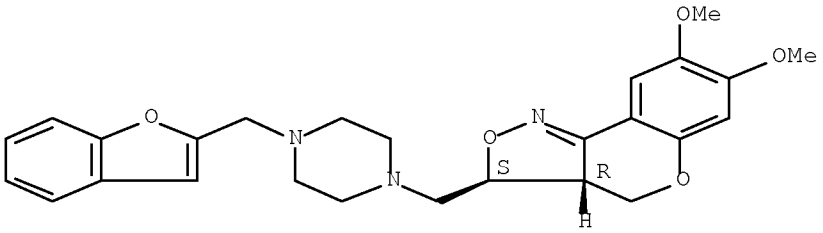
Relative stereochemistry.



●2 HCl

RN 452316-03-9 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-(2-benzofuranylmethyl)-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, dihydrochloride, (3R,3aS)-rel- (9CI) (CA INDEX NAME)

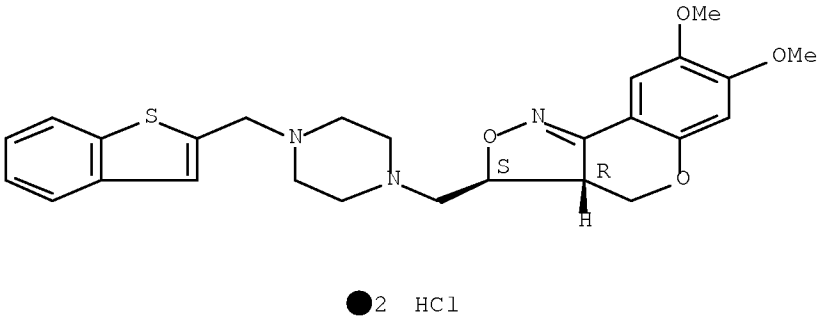
Relative stereochemistry.



●2 HCl

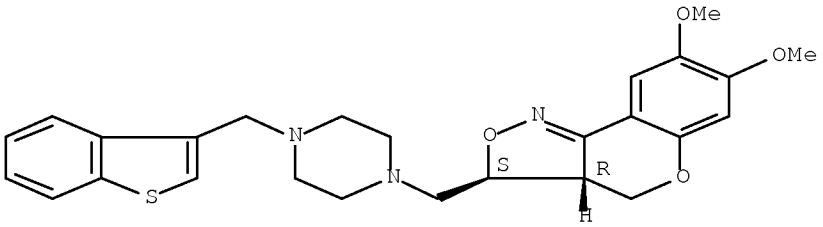
RN 452316-06-2 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-(benzo[b]thien-2-ylmethyl)-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, dihydrochloride, (3R,3aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

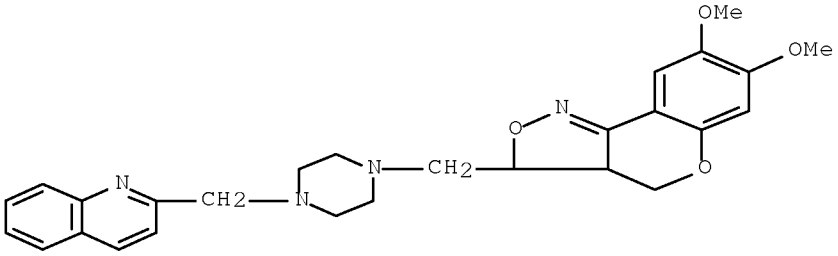


RN 452316-09-5 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-(benzo[b]thien-3-ylmethyl)-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.

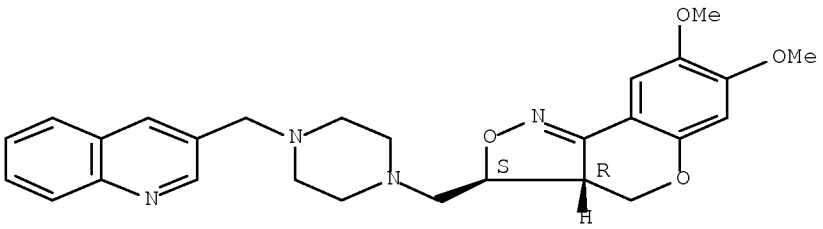


RN 452316-12-0 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-7,8-dimethoxy-3-[[4-(2-quinolinylmethyl)-1-piperazinyl]methyl]- (CA INDEX NAME)



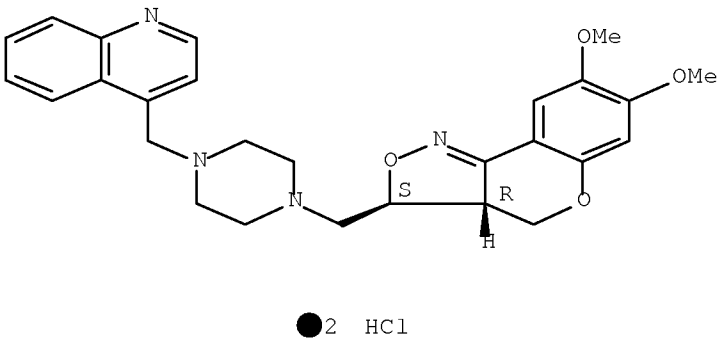
RN 452316-15-3 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-7,8-dimethoxy-3-[[4-(3-quinolinylmethyl)-1-piperazinyl]methyl]-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



RN 452316-18-6 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3a,4-dihydro-7,8-dimethoxy-3-[[4-(4-quinolinylmethyl)-1-piperazinyl]methyl]-, dihydrochloride, (3R,3aS)-rel- (9CI) (CA INDEX NAME)

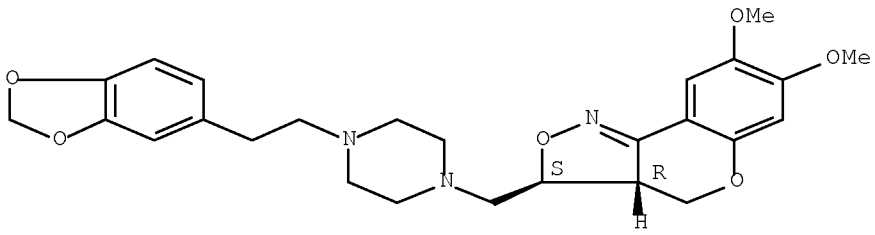
Relative stereochemistry.



●2 HCl

RN 452316-24-4 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-[2-(1,3-benzodioxol-5-yl)ethyl]-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, dihydrochloride, (3R,3aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

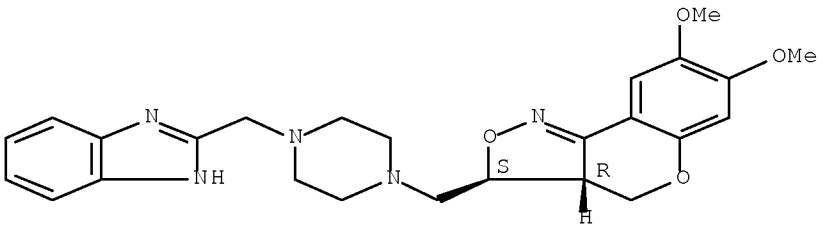


●2 HCl

RN 452316-39-1 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-(1H-benzimidazol-2-ylmethyl)-1-

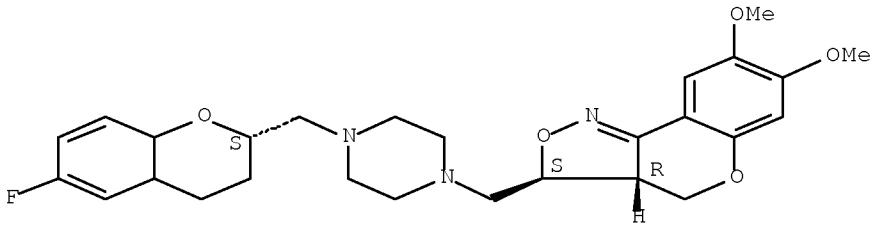
piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



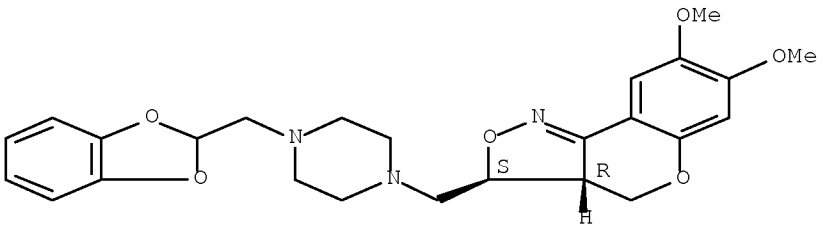
RN 452316-58-4 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-[[(2R)-6-fluoro-3,4,4a,8a-tetrahydro-2H-1-benzopyran-2-yl]methyl]-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, (3R,3aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 452316-64-2 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-(1,3-benzodioxol-2-ylmethyl)-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX NAME)

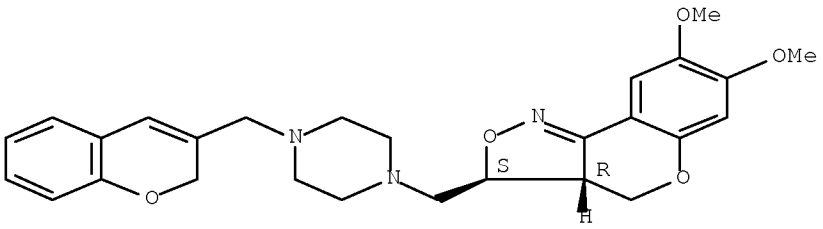
Relative stereochemistry.



RN 452318-91-1 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-(2H-1-benzopyran-3-ylmethyl)-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX

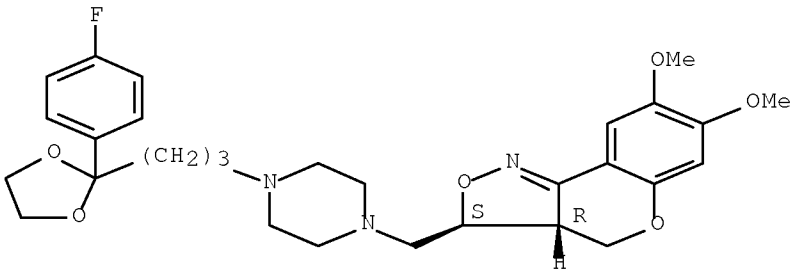
NAME)

Relative stereochemistry.



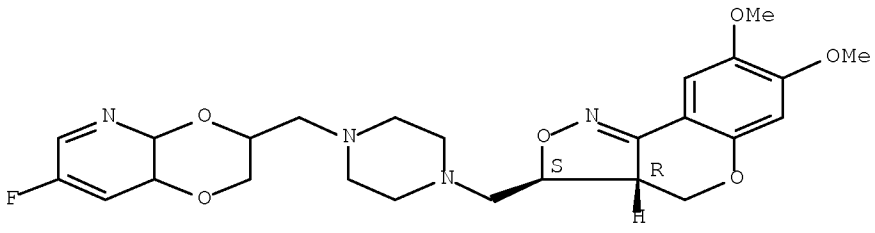
RN 452319-17-4 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-[3-[2-(4-fluorophenyl)-1,3-dioxolan-2-yl]propyl]-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



RN 452934-93-9 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-[(7-fluoro-2,3,4a,8a-tetrahydro-1,4-dioxino[2,3-b]pyridin-3-yl)methyl]-1-piperazinyl]methyl]-3a,4-dihydro-7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX NAME)

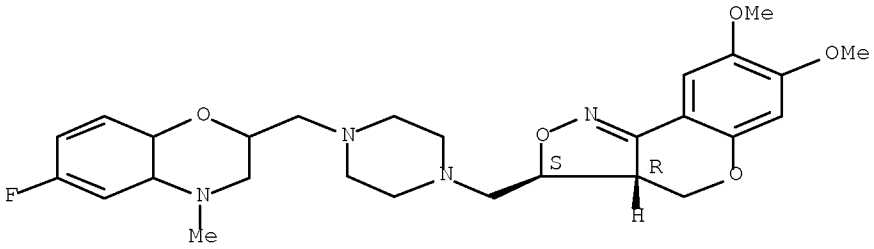
Relative stereochemistry.



RN 452934-94-0 HCAPLUS
CN 3H-[1]Benzopyrano[4,3-c]isoxazole, 3-[[4-[(6-fluoro-3,4,4a,8a-tetrahydro-4-methyl-2H-1,4-benzoxazin-2-yl)methyl]-1-piperazinyl]methyl]-3a,4-dihydro-

7,8-dimethoxy-, (3R,3aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



IC ICM C07D498-04
ICS C07D261-20; A61K031-495; A61P025-00
CC 28-6 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT 452313-36-9P 452313-40-5P 452313-43-8P 452313-46-1P
452313-50-7P 452313-54-1P 452313-56-3P 452313-61-0P 452313-65-4P
452313-74-5P 452313-77-8P 452313-85-8P 452313-88-1P 452313-91-6P
452313-93-8P 452313-98-3P 452314-01-1P 452314-05-5P 452314-08-8P
452314-11-3P 452314-14-6P 452314-16-8P 452314-18-0P 452314-20-4P
452314-23-7P 452314-26-0P 452314-29-3P 452314-31-7P 452314-34-0P
452314-37-3P 452314-40-8P 452314-43-1P 452314-46-4P 452314-49-7P
452314-52-2P 452314-55-5P 452314-57-7P 452314-60-2P 452314-62-4P
452314-65-7P 452314-68-0P 452314-71-5P 452314-74-8P 452314-77-1P
452314-80-6P 452314-83-9P 452314-86-2P 452314-89-5P 452314-92-0P
452314-95-3P 452314-98-6P 452315-01-4P
452315-04-7P 452315-07-0P 452315-10-5P
452315-13-8P 452315-16-1P 452315-19-4P
452315-22-9P 452315-24-1P 452315-27-4P
452315-30-9P 452315-33-2P 452315-36-5P 452315-38-7P
452315-40-1P 452315-42-3P 452315-44-5P 452315-46-7P 452315-48-9P
452315-51-4P 452315-52-5P 452315-55-8P 452315-58-1P 452315-61-6P
452315-63-8P 452315-66-1P 452315-70-7P 452315-73-0P 452315-76-3P
452315-79-6P 452315-82-1P 452315-85-4P 452315-87-6P 452315-90-1P
452315-92-3P 452315-94-5P 452315-97-8P
452316-00-6P 452316-03-9P 452316-06-2P
452316-09-5P 452316-12-0P 452316-15-3P
452316-18-6P 452316-21-1P 452316-24-4P 452316-27-7P
452316-30-2P 452316-33-5P 452316-36-8P 452316-39-1P
452316-42-6P 452316-45-9P 452316-48-2P 452316-51-7P 452316-53-9P
452316-55-1P 452316-58-4P 452316-64-2P 452316-66-4P
452316-69-7P 452316-72-2P 452316-75-5P 452316-81-3P 452316-84-6P
452316-87-9P 452316-89-1P 452316-91-5P 452316-93-7P 452316-95-9P
452316-97-1P 452316-99-3P 452317-02-1P 452317-04-3P 452317-06-5P
452317-08-7P 452317-10-1P 452317-12-3P 452317-14-5P 452317-16-7P
452317-18-9P 452317-20-3P 452317-22-5P 452317-24-7P 452317-26-9P
452317-28-1P 452317-30-5P 452317-32-7P 452317-34-9P 452317-36-1P
452317-38-3P 452317-40-7P 452317-42-9P 452317-44-1P 452317-46-3P
452317-48-5P 452317-50-9P 452317-52-1P 452317-54-3P 452317-56-5P
452317-58-7P 452317-60-1P 452317-64-5P 452317-67-8P 452317-69-0P
452317-71-4P 452317-73-6P 452317-76-9P 452317-79-2P 452317-82-7P
452317-84-9P 452317-86-1P 452317-89-4P 452317-92-9P 452317-94-1P
452317-96-3P 452317-99-6P 452318-02-4P 452318-04-6P 452318-07-9P
452318-09-1P 452318-11-5P 452318-13-7P 452318-15-9P 452318-18-2P

452318-20-6P 452318-22-8P 452318-24-0P 452318-27-3P 452318-30-8P
452318-32-0P 452318-34-2P 452318-36-4P 452318-38-6P 452318-41-1P
452318-43-3P 452318-45-5P 452318-47-7P 452318-49-9P 452318-52-4P
452318-54-6P 452318-57-9P 452318-60-4P 452318-63-7P 452318-65-9P
452318-67-1P 452318-69-3P 452318-71-7P 452318-73-9P 452318-75-1P
452318-77-3P 452318-79-5P 452318-81-9P 452318-83-1P 452318-85-3P
452318-87-5P 452318-89-7P 452318-91-1P 452318-93-3P
452318-95-5P 452318-97-7P 452318-99-9P 452319-01-6P 452319-03-8P
452319-05-0P 452319-07-2P 452319-09-4P 452319-11-8P 452319-13-0P
452319-15-2P 452319-17-4P 452319-20-9P 452319-22-1P
452319-24-3P 452319-25-4P 452319-27-6P 452319-29-8P 452319-31-2P
452319-33-4P 452319-35-6P 452319-37-8P 452319-39-0P 452319-41-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation and pharmaceutical activity of substituted isoxazolines as anti-depressants)

IT 452319-43-6P 452319-45-8P 452319-47-0P 452319-49-2P 452319-51-6P
452319-53-8P 452319-55-0P 452319-57-2P 452319-59-4P 452319-61-8P
452319-63-0P 452319-65-2P 452319-67-4P 452319-69-6P 452319-71-0P
452319-73-2P 452319-75-4P 452319-77-6P 452319-78-7P 452319-80-1P
452319-81-2P 452319-83-4P 452319-85-6P 452319-87-8P 452319-89-0P
452319-91-4P 452319-93-6P 452319-95-8P 452319-97-0P 452319-99-2P
452320-01-3P 452320-03-5P 452320-06-8P 452320-07-9P 452320-09-1P
452320-11-5P 452320-13-7P 452320-15-9P 452320-17-1P 452320-19-3P
452320-21-7P 452320-23-9P 452320-25-1P 452320-27-3P 452320-29-5P
452320-31-9P 452320-34-2P 452320-36-4P 452320-38-6P 452320-40-0P
452320-42-2P 452320-44-4P 452320-46-6P 452320-48-8P 452320-50-2P
452320-52-4P 452320-54-6P 452320-56-8P 452320-58-0P 452320-60-4P
452320-62-6P 452320-64-8P 452320-66-0P 452320-68-2P 452320-70-6P
452320-72-8P 452320-74-0P 452320-76-2P 452320-78-4P 452320-80-8P
452320-82-0P 452320-84-2P 452320-86-4P 452320-88-6P 452320-90-0P
452320-92-2P 452320-94-4P 452320-96-6P 452320-98-8P 452321-00-5P
452321-02-7P 452321-04-9P 452321-06-1P 452321-08-3P 452321-10-7P
452321-12-9P 452321-14-1P 452321-16-3P 452321-19-6P 452321-21-0P
452321-23-2P 452321-25-4P 452321-27-6P 452321-29-8P 452321-31-2P
452321-33-4P 452321-35-6P 452321-37-8P 452321-39-0P 452321-41-4P
452321-43-6P 452321-45-8P 452321-47-0P 452321-49-2P 452321-51-6P
452321-53-8P 452321-55-0P 452321-57-2P 452321-59-4P 452321-61-8P
452934-93-9P 452934-94-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation and pharmaceutical activity of substituted isoxazolines as anti-depressants)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

***** SEARCH HISTORY *****

```
=> d his nofile

     (FILE 'HOME' ENTERED AT 13:54:20 ON 21 FEB 2008)

     FILE 'HCAPLUS' ENTERED AT 13:54:29 ON 21 FEB 2008
L1             1 SEA ABB=ON  PLU=ON  US20060122167/PN
                 D L1 IBIB AB IT

     FILE 'REGISTRY' ENTERED AT 13:55:17 ON 21 FEB 2008
L2               STRUCTURE UPLOADED
                 D
L3             1 SEA SSS SAM L2
                 D SCAN

     FILE 'STNGUIDE' ENTERED AT 13:57:16 ON 21 FEB 2008

     FILE 'REGISTRY' ENTERED AT 14:01:26 ON 21 FEB 2008
L4               STRUCTURE UPLOADED
                 D
L5             0 SEA SSS SAM L4
L6             8 SEA SSS FUL L2
                 D SCAN

     FILE 'STNGUIDE' ENTERED AT 14:04:15 ON 21 FEB 2008

     FILE 'REGISTRY' ENTERED AT 14:09:22 ON 21 FEB 2008
L7               STRUCTURE UPLOADED
L8             0 SEA SUB=L6 SSS SAM (L4 OR L7)
L9             0 SEA SUB=L6 SSS FUL (L4 OR L7)

     FILE 'HCAPLUS' ENTERED AT 14:12:12 ON 21 FEB 2008
L10            7 SEA ABB=ON  PLU=ON  L6
L11            0 SEA ABB=ON  PLU=ON  L10 AND L1

     FILE 'STNGUIDE' ENTERED AT 14:13:17 ON 21 FEB 2008

     FILE 'REGISTRY' ENTERED AT 14:19:12 ON 21 FEB 2008
L12              STRUCTURE UPLOADED
                 D
L13           50 SEA SSS SAM L12
L14            1 SEA SUB=L6 SSS SAM L12
                 D SCAN
L15         2772 SEA SSS FUL L12

     FILE 'HCAPLUS' ENTERED AT 14:24:53 ON 21 FEB 2008
L16          206 SEA ABB=ON  PLU=ON  L15
L17            1 SEA ABB=ON  PLU=ON  L16 AND L1

     FILE 'REGISTRY' ENTERED AT 14:25:16 ON 21 FEB 2008
L18            1 SEA SUB=L15 SSS SAM (L4 OR L7)
L19           16 SEA SUB=L15 SSS FUL (L4 OR L7)
                 D SCAN

     FILE 'STNGUIDE' ENTERED AT 14:26:37 ON 21 FEB 2008

     FILE 'REGISTRY' ENTERED AT 14:29:05 ON 21 FEB 2008
                 SAVE TEMP L15 SHT989REGL4/A
```

```
     FILE 'HCAPLUS' ENTERED AT 14:30:27 ON 21 FEB 2008
L20           2 SEA ABB=ON  PLU=ON  L19
                D SCAN TI HIT
L21           1 SEA ABB=ON  PLU=ON  L20 AND L1
                SAVE TEMP L20 SHT989HCAP/A

     FILE 'REGISTRY' ENTERED AT 14:31:45 ON 21 FEB 2008
L22           0 SEA ABB=ON  PLU=ON  L19 AND (MEDLINE/LC OR BIOSIS/LC OR
                DRUGU/LC OR EMBASE/LC)
                D QUE L20

     FILE 'HCAPLUS' ENTERED AT 14:33:42 ON 21 FEB 2008
                D L20 IBIB ED ABS HITSTR HITIND 1-2

     FILE 'REGISTRY' ENTERED AT 14:33:43 ON 21 FEB 2008

L23             STRUCTURE UPLOADED
                D
L24           2 SEA SUB=L15 SSS SAM (L4 OR L23)
                D SCAN
L25          37 SEA SUB=L15 SSS FUL (L4 OR L23)

     FILE 'HCAPLUS' ENTERED AT 14:49:39 ON 21 FEB 2008
L26           3 SEA ABB=ON  PLU=ON  L25
                D QUE L26
                D L26 IBIB ED ABS HITSTR HITIND 1-3
```